

**I. Objections to Specification/Claims**

The Examiner has objected to the specification and claims for several reasons.

(1) The Examiner has objected to the claims stating that the claims were mis-numbered when filed and that claims 23-28 should be 22-27. Applicants acknowledge this error and thank the Examiner for renumbering the claims.

(2) The Examiner has objected to the specification stating that the abbreviation LBU appears for the first time on page 6 but is not spelled out in full on page 6. In response, Applicants have amended the specification to indicate on page 6 that LBU is an abbreviation for Lytic Base Unit. Support for this amendment is found on page 11, paragraph 29, line 5.

(3) The Examiner has also objected to the specification stating that the phrase " $5500^{-1}$  m  $\text{cm}^{-1}$ " is incorrect and should be changed to " $5500^{-1}$  M  $\text{cm}^{-1}$ ". In response, Applicants have made the suggested change.

(4) In addition, the Examiner has objected to claim 27 stating that the phrase "wherein microbial growth in resistant" should be changed to "wherein microbial growth is resistant". In response, Applicants have amended claim 27 to effectuate this change.

Applicants believe they have fully responded to the Examiner's objections and request that the objections be withdrawn.

**II. Drawings:**

The Examiner has stated that the drawings filed on February 16, 2001 are acceptable subject to correction of the informalities indicated in the "Notice of Draftperson's Patent Review". In response, Applicants submit herewith revised drawings 1, 8, 10 and 12 which incorporate changes responsive to the "Notice of Draftperson's Patent Review". Applicants

assert that the Drawings are proper and should be acceptable to the Examiner. Therefore, Applicants respectfully request that any objections to the drawings be withdrawn.

III. Claim rejections under 35 U.S.C. § 112, second paragraph:

The Examiner has rejected claims 1-27 under 35 U.S.C. § 112, second paragraph as indefinite for the following reasons:

The Examiner alleges that the term "having" in claim 1 is indefinite because it is open-ended, suggesting the use of the closed term "consisting of". Applicants respectfully disagree that claim 1 is indefinite. The specification clearly teaches that the peptides of the present invention may be linked to a cargo. The cargo may be an amino acid sequence (such as the amino acid sequence of lysozyme). See page 25-26, paragraph 65. The cargo may also be another peptide of the invention because the specification teaches that the cargo may be another factor which has antimicrobial activity, which encompasses other peptides of the present invention. As such, the use of the term having is fully consistent with the teachings of the specification and is definite in light of the specification. Therefore, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, second paragraph be withdrawn.

The Examiner further alleges that the recitation of the term "one or more peptides" in claim 2 is indefinite because it encompasses any number of peptides greater than one. Applicants respectfully disagree. However, Applicants have amended claim 2 to make clear that the claim is directed to "one or more of the following peptides

RVIRVVQRACRAIRHIVRRIRQGLRRIL (SEQ ID NO: 1);

RVIRVVQRACRAIRHIVRRIRQGLRRILRVV (SEQ ID NO: 2); and

RWIRVVQRWCRAIRHIWRRIRQGLRRWLRVV (SEQ ID NO: 3)."

Therefore, Applicants respectfully request that the rejection of claim 2 under 35 U.S.C. § 112, second paragraph be withdrawn.

In addition, the Examiner alleges that the phrase "low salt" is indefinite in claim 10. Applicants have amended claim 10 to recite the phrase "a low salt medium" as suggested by the Examiner. Support for this amendment is found throughout the specification and specifically by Figure 3, and page 8, paragraph 16 and page 33, paragraph 81. Therefore, Applicants respectfully request withdrawal of the rejection of claim 10 under 35 U.S.C. § 112, second paragraph.

The Examiner further alleges that the phrase "at least one peptide" in claim 12 and renumbered claim 24 is indefinite because it is not clear whether one, two or three peptides are included in the solid phase substrate. Applicants respectfully disagree that claim 12 and renumbered claim 24 are indefinite. The Examiner has demonstrated the definiteness of the claims in the rejection by acknowledging the finite number of possibilities – 7 to be exact. The claims indicate that peptides having SEQ ID NOs: 1, 2 or 3 may be used alone, in combination of any two peptides (1 and 2; 1 and 3; or 2 and 3) or all three peptides together. Therefore, Applicants respectfully request that the rejection of claim 12 and 24 under 35 U.S.C. § 112, second paragraph be withdrawn.

The Examiner has rejected claim 13 for improper antecedent basis of the phrase "the solid phase of claim 12". Applicants have amended this phrase in claim 13 to "the solid phase substrate of claim 12" thereby correcting the incorrect antecedent basis. No new matter has been added by this amendment.

The Examiner has also rejected claim 18 as indefinite for reciting the phrase "at least one cysteine" alleging that because the peptides of claim 1 have only one cysteine, this phrase is

indefinite. Applicants respectfully disagree. Claim 1 is directed to a peptide having the amino acid sequence of SEQ ID NOs 1, 2 and 3. As Applicants have indicated above, the peptides of claim 1 may include other amino acids and therefore, claim 18 is not indefinite because the additional amino acids may be cysteines. Therefore, Applicants respectfully request that the rejection of claim 18 under 35 U.S.C. § 112, second paragraph be withdrawn.

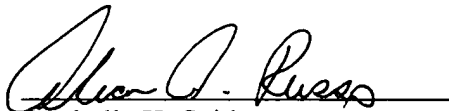
IV. Claim rejections under obviousness type double patenting

The Examiner has provisionally rejected claims 1-27 for obviousness type double patenting alleging that the claims conflict with claims 1-7, 26-28, 35-42, 50, 54, 56 and 62 of Application serial no. 10/079,075. Applicants believe that this rejection is better suited for Application serial no. 10/079,075 when it is examined. However, Applicants file concurrently herewith a Preliminary Amendment for Application serial no. 10/079,075 in which the claims have been amended to delete any overlapping subject matter, making the provisional rejection for obviousness type double patenting moot. Therefore, Applicants respectfully request that the rejection of claims 1-27 for obviousness type double patenting be withdrawn.

V. Conclusion

In view of the technical amendments and remarks made herein, and in view of the Preliminary Amendment filed concurrently herewith for U.S. Application serial no. 10/079,075, Applicants respectfully submit that the claims are presently in condition for allowance. Favorable reconsideration of this application is therefore earnestly solicited.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Page 6: Please rewrite paragraph 9 as follows:

In another embodiment of the invention, the antimicrobial peptides are LLP1 analogs having modifications based on the following principles: (i) optimizing amphipathicity, (ii) substituting arginine (Arg) on the charged face and/or valine (Val) or tryptophan (Trp) on the hydrophobic face with another amino acid, and (iii) increasing peptide length (referred to collectively herein as Lytic Base Unit (LBU) peptides, *e.g.* LBU-2, SEQ ID NO:4; LBU-3, SEQ ID NO:5; LBU-3.5, SEQ ID NO:6; LBU-4, SEQ ID NO:7; WLBU-1, SEQ ID NO:8, WLBU-2, SEQ ID NO:9, WLBU-3, SEQ ID NO:10; and WLBU-4, SEQ ID NO:11; *see* Table 1). The LBU peptides deviate greatly from the parent LLPI, for example, LBU-2 and LBU-3 deviate from the parent LLP1 sequence by greater than 90%.

Page 18-19: Please rewrite paragraph 45 as follows:

~~[0002]~~ Peptide concentration is quantitated using a standard ninhydrin colorimetric assay (*see* Example 1 below). A standard curve using a Leu standard is generated by reading the spectrophotometric absorbance at 570 nm of increasing volumes of the leucine stock combined with the commercially available (Dupont) ninhydrin reagents on a spectrophotometer. The readings of peptide samples are compared to the leucine standard curve to quantitate the amount of peptide in each sample. Alternatively, if the peptide contains Trp in its sequence, peptide concentration can be determined by UV spectroscopy using a molar extinction coefficient  $\epsilon_{280} = 5500^{-1} [\text{m}] \text{MAcm}^{-1}$ .

IN THE CLAIMS

Please rewrite claims, 2, 10, 13 and 27 as follows:

2. (Amended) 2. A composition comprising one or more [peptides of claim 1] of the following peptides:

RVIRVVQRACRAIRHIVRRIRQGLRRIL (SEQ ID NO: 1);

RVIRVVQRACRAIRHIVRRIRQGLRRILRVV (SEQ ID NO: 2); and

RWIRVVQRWCRAIRHIWRRIRQGLRRWLRVV (SEQ ID NO: 3),

and a carrier.

10. (Amended) The peptide of claim 1 wherein said peptide has antimicrobial activity in a low salt medium.

13. The solid phase substrate of claim 12 wherein the peptide is  
RVIRVVQRACRAIRHIVRRIRQGLRRIL (SEQ ID NO: 1).

27. (Amended) The method of claim 23 or 25 wherein said microbial growth [in] is resistant to antibiotics.